

## Claims:

1. A method of treating a protein conformational disorder in  
5 an individual comprising:  
stimulating autophagy activity in the individual.
2. A method according to claim 1 wherein the protein  
conformational disorder is characterised by cytoplasmic  
10 - protein aggregation.
3. A method according to claim 1 or claim 2 comprising  
administering an autophagy-inducing agent to said individual.
- 15 4. A method according to claim 3 wherein the autophagy  
inducing agent is an mTOR inhibitor.
5. A method according to claim 3 or claim 4 wherein the  
autophagy-inducing agent is a rapamycin macrolide.  
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6. A method according to claim 5 wherein the rapamycin  
macrolide is rapamycin.
7. A method according to claim 5 wherein the rapamycin  
25 macrolide is a rapamycin analogue.
8. A method according to claim 7 wherein the rapamycin  
analogue is selected from the group consisting of CCI-779, 40-  
O-(2-hydroxy)ethyl-rapamycin, 32-deoxo-rapamycin, 16-O-pent-2-  
30 ynyl-32-deoxo-rapamycin, 16-O-pent-2-ynyl-32-deoxo-40-O-(2-  
hydroxyethyl)-rapamycin, 16-O-pent-2-ynyl-32-(S)-dihydro-  
rapamycin and 16-O-pent-2-ynyl-32-(S)-dihydro-40-O-(2-  
hydroxyethyl)-rapamycin .
- 35 9. A method according to any one of the preceding claims  
wherein the disorder is a codon reiteration mutation disorder.

10. A method according to claim 9 wherein the disorder is a polyQ expansion disorder.
11. A method according to claim 10 wherein the polyQ expansion disorder is selected from the group consisting of Huntington's disease, spinocerebellar ataxias types 1, 2, 3, 6, 7, and 17, Kennedy's disease and dentatorubral-pallidoluysian atrophy.
12. A method according to claim 9 wherein the disorder is a polyA expansion disorder.
13. A method according any one of claims 1 to 8 wherein the disorder is an  $\alpha$ -synucleiopathy.
14. A method according to claim 13 wherein the disorder is selected from the group consisting of Parkinson's disease, LB variant Alzheimer's disease and LB dementia.
15. A method according to any one of claims 1 to 8 wherein the disorder is a prion disorder.
16. A method according to claim 15 wherein the prion disorder is CJD.
17. Use of an autophagy-inducing agent in the manufacture of a medicament for use in the treatment of a protein conformational disorder in an individual.
18. Use according to claim 17 wherein the protein conformational disorder is characterised by cytoplasmic protein aggregation.
19. Use according to claim 17 or claim 18 wherein the autophagy-inducing agent is an mTOR inhibitor.

20. Use according to any one of claims 17 to 19 wherein autophagy-inducing agent is a rapamycin macrolide.
21. Use according to claim 20 wherein the rapamycin macrolide is rapamycin.
22. Use according to claim 20 wherein the rapamycin macrolide is a rapamycin analogue.
23. Use according to claim 22 wherein the analogue is selected from the group consisting of CCI-779, 40-O-(2-hydroxy)ethyl-rapamycin, 32-deoxo-rapamycin, 16-O-pent-2-ynyl-32-deoxo-rapamycin, 16-O-pent-2-ynyl-32-deoxo-40-O-(2-hydroxyethyl)-rapamycin, 16-O-pent-2-ynyl-32-(S)-dihydro-rapamycin and 16-O-pent-2-ynyl-32-(S)-dihydro-40-O-(2-hydroxyethyl)-rapamycin
24. Use according to any one of claims 17 to 23 wherein the disorder is a codon reiteration mutation disorder.
25. Use according to claim 24 wherein the disorder is a polyQ expansion disorder.
26. Use according to claim 25 wherein the polyQ expansion disorder is selected from the group consisting of Huntington's disease, spinocerebellar ataxias types 1, 2, 3, 6, 7, and 17, Kennedy's disease and dentatorubral-pallidoluysian atrophy.
27. Use according to claim 26 wherein the disorder is a polyA expansion disorder.
28. Use according to any one of claims 17 to 23 wherein the disorder is an  $\alpha$ -synucleiopathy.
29. Use according to claim 28 wherein the disorder is selected from the group consisting of Parkinson's disease, LB variant Alzheimer's disease and LB dementia.

30. Use according any one of claims 17 to 23 wherein the disorder is a prion disorder.

5 31. Use according to claim 30 wherein the prion disorder is CJD.

32. A method of identifying an agent useful in the treatment of a protein conformational disorder comprising;  
10 contacting a mammalian cell with a test compound; and,  
determining the autophagy activity of said cell,  
an increase in autophagy activity in the presence of said compound being indicative that the compound is a candidate agent for use in the treatment of a protein conformational  
15 disorder.

33. A method according to claim 32 wherein the cell comprises a heterologous nucleic acid encoding an aggregation-prone polypeptide.

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34. A method according to claim 33 wherein said heterologous nucleic acid is operably linked to an inducible promoter.

35. A method according to claim 33 or claim 34 comprising  
25 expressing said nucleic acid and stopping said expression, prior to contacting the mammalian cell with the test compound.

36. A method according to any one of claims 31 to 35 comprising modifying the compound to optimise the  
30 pharmaceutical properties thereof

37. A method comprising formulating the test compound into a pharmaceutical composition.

35 38. A method of producing an agent for the treatment of a protein conformational disorder comprising;

modifying rapamycin to produce a rapamycin derivative; and;  
determining the autophagy inducing activity of said  
derivative.

- 5 39. A method according to claim 38 comprising determining the  
ability of said derivative to inhibit mTOR.

40. A method according to claim 38 or claim 39 comprising  
determining the ability of said derivative to enhance the